REMARKS

Upon entry of the present amendments, claims 1-3, 6, and 13-14 will be pending in the application. Claim 1 has been amended to more particularly define the claimed invention and to correct various typographical errors. Support for the amendments to claim 1 can be found at least at, *e.g.*, page 13, line 29 through page 14, line 5 and at page 15, lines 15-17. Thus, no new matter has been added.

Claim Rejections -- 35 U.S.C. § 112

Claims 1-3, 6, 13 and 14 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. According to the Examiner, the amended claims submitted on August 24, 2005 include new matter. Specifically, the Examiner has rejected claim 1 for reciting the limitation transplanting "at least about $1x10^6$ mitogenic growth factor-responsive neural stem cells", because the specification does not contemplate transplanting "at least about $1x10^6$" cells. (*See* Office Action at page 3).

Applicant thanks the Examiner for pointing out this discrepancy. Claim 1 has been amended herein to specify "a method for transplanting one or more deposits of about 500,000 cells". Support for this amendment is found at least at, *e.g.*, page 15, lines 15-17 and page 31, lines 22-25. As this claim no longer recites the limitation "at least about $1x10^6$ mitogenic growth factor-responsive neural stem cells", Applicant submits that this rejection has been overcome and should be withdrawn.

The Examiner has also indicated that the recitation of the limitation "said first area comprising multiple loci for receiving an aliquot of the neural stem cells" in claim 1 also constitutes new matter. (*See* Office Action at page 4). In response, Applicant has deleted this limitation from claim 1. Thus, this rejection is moot and should be withdrawn.

Moreover, Applicant notes that amended claim 1 now refers to "multiple deposits" rather than "multiple loci". As acknowledged by the Examiner, this limitation is supported by the specification at page 15, line 16. (*See* Office Action at page 4). Thus, Applicant submits that the inclusion of this limitation in claim 1, as amended herein, does not constitute new matter.

The Examiner has also rejected claims 1-3, 6, 13, and 14 under 35 U.S.C. § 112, first paragraph for lack of enablement. According to the Examiner, "undue experimentation would have been required to develop protocols within the scope of the claims that produce a therapeutic effect in a diseased animal." (Office Action at page 6). Moreover, the Examiner also states that Applicant has provided no support for the assertion that the post-filing references used "substantially identical methods" to those of the claimed invention. (*See* Office Action at page 8). Applicant traverses.

The Standard for Enablement

In determining whether a particular disclosure satisfies the enablement requirement the factors to be considered are set forth in *In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Here, Applicant submits that the *Wands* factors are met. A plain reading of the instant specification shows that it contains a detailed disclosure commensurate in scope with the protection sought by the claims, as amended. Moreover, as demonstrated below, the specification and Examples, taken as a whole (and taken in conjunction with the post-filing references discussed in detail below), teach those of ordinary skill in the art how to use the claimed methods without undue experimentation.

The Teachings of the Specification

Contrary to the Examiner's position, the specification and the voluminous evidence of record demonstrate that the ordinarily skilled artisan could use the claimed invention without undue experimentation. Accordingly, one of ordinary skill in the art would be able to routinely use the methods described in the application to transplant one or more deposits of about 500,000 cells grown as neurospheres which contain neural stem cells that are capable of differentiating into neurons, oligodendrocytes, or astrocytes, at a first locus to achieve migration of the transplanted neural stem cells via infusion of a mitogenic growth factor at a second locus, as now recited by claim 1, as amended herein. According to these methods, the transplanted cells retain their responsiveness to the mitogenic growth factor *in vivo*, as well as the ability to differentiate into neurons, oligodendrocytes, or astrocytes. Support for this claimed method is found throughout the specification (*see* Specification pages 14-16), and particularly within Example 15

(*see, e.g.*, Specification, page 31, line 23 through page 32, line 3; page 35, line 24 through page 36 line 2; page 37, lines 1-9; and page 41, lines 11-12.)

Moreover, as indicated by the instant specification, *in vivo* regulation of neural stem cells transplanted into the brain via local delivery of a neurotrophic factor is able to guide cell migration and/or differentiation. These claimed techniques increase graft survival, promotes reinnervation of host tissue (as well as the associated behavioral recovery), and enhances the effectiveness of neural stem cell transplantation as a restorative therapy for treating neurodegenerative diseases. (*See, e.g.*, Specification, page 41, lines 12-17). Applicant asserts that such results are indicative of a therapeutic benefit or effect achieved by the claimed methods.

Thus, Applicant submits that there is ample intrinsic evidence of record that demonstrates how to transplant specific cells that are known to have the ability to migrate and/or differentiate in response to a mitogenic growth factor (*e.g.*, neural stem cells) into the brain of a living host subject, thereby increasing graft survival and enhancing the effectiveness of the transplantation, while maintaining the cells' ability to subsequently differentiate into neurons, oligodendrocytes, or astrocytes. (*See, e.g.*, Specification, page 6, line 24 through page 7, line 7; page 15, line 22; page 15, line 26 through page 16; line 16; and Examples 9 and 15).

Working Examples

As noted previously, Applicant has also provided several working examples (*e.g.*, Examples 8, 9, and 15), which, when taken together, illustrate the methods of the claimed invention such that one of ordinary skill in the art could practice the claimed invention without undue experimentation. Applicant contends that these working examples correlate with the steps recited in the claimed methods. Thus, Applicant submits that no undue experimentation is required to practice the methods recited by the claims.

Level of Skill in the Art and Quantity of Experimentation

Furthermore, Applicant also notes that the state of the prior art was such that administering the neural stem cell and tissue protocols were well known to the ordinarily skilled artisan at the priority date of this case. As is plain from the voluminous evidence already of record, multiple scientific publications confirm that transplantation of neural stem cells can be

routinely achieved. [1/] Furthermore, Applicant contends that the ordinarily skilled artisan would recognize that such transplantation results in a therapeutic benefit to the host.

Applicant does not believe that the law requires the demonstration of a therapeutic benefit. *See*, Decision on Appeal in Appeal No. 2005-2594, decided March 31, 2006 (courtesy copy enclosed). Applicant submits that the claims, as amended herein, are fully enabled by the as-filed specification. As such, this rejection should be withdrawn.

Claims 1-3, 6, 13, and 14 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in their recitation of the phrase "selected from the group consisting of neurons, astrocytes, or oligodendrocytes." (Office Action at pages 8-9 (emphasis added)). As suggested by the Examiner, the "or" in this phrase in claim 1 has been replaced by "and". As such, Applicant believes that this rejection has been overcome and should be withdrawn.

1/ *See, e.g.*, Qu et al., Ageing 12:1127-32 (2001) ("Qu"); Akiyama et al., Exp. Neurol. 167:27-39 (2001) ("Akiyama"); Kurimoto et al., Neuroscience Letters 306:57-60 (2001) ("Kurimoto"); Nishida et al., Investigative Ophthalmology & Visual Science 41:4268-74 (2000) ("Nishida"); Reubinoff et al., Nature Biotech 19:1134-40 (2001) ("Reubinoff"); Mitome et al., Brain 124:2147-61 (2001) ("Mitome"); Milward et al., J. Neurosci. Res. 50:862-71 (1997) ("Milward"); Zhang et al., Proc. Natl. Acad. Sci. USA 96:4089-94 (1999) ("Zhang"); Brustle et al., Nature Biotechnol. 16:1040-44 (1998) ("Brustle"); Yandava et al., Proc. Natl. Acad. Sci. USA 96:7029-34 (1999) ("Yandava"); Flax et al., Nature Biotechnol., 16:1033-39 (1993) ("Flax"); Fricker et al., J. Neurosci. 19:5990-6005 (1999) ("Fricker"); Aboody et al., Proc. Natl. Acad. Sci. USA 97:12846-51 (2000) ("Aboody"); Temple et al., Nature 414:112-17 (2001) ("Temple"); Pluchino *et al.*, Nature 422:688-94 (2003) ("Pluchino"); Ishibashi et al., J. Neurosci. Res. 78:215-23 (2004) ("Ishibashi"); Ogawa et al., J. Neurosci. Res. 69:925-33 (2002) ("Ogawa"); and Cummings, et al., Proc. Natl Acad. Sci. 102(39):14069-74 (2005) ("Cummings") (courtesy copy enclosed).

CONCLUSION

Applicants submit that this paper is fully responsive and that the application is in condition for allowance. Such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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Ivor R. Elrifi, Reg. No. 39,529
Christina K. Stock, Reg. No. 45,899
Attorneys for Applicant
Telephone: (617) 542-6000
Facsimile: (617) 542-2241
Customer Number **30623**.